25

30

WHAT IS CLAIMED IS:

1. A compound of Formula (I):

5 or an optical isomer, enantiomer, diastereomer, racemate or racemic mixture thereof, ester, prodrug form, or a pharmaceutically acceptable salt thereof, wherein

A is selected from aryl, heterocyclyl, and $C_1\text{-}C_{10}$ alkyl, said aryl, heterocyclyl, and $C_1\text{-}C_{10}$ alkyl being optionally substituted with one or more members selected from the group consisting of halogen, OH, aryl, $C_3\text{-}C_8$ cycloalkyl, $C_1\text{-}C_{10}$ alkyl substituted with a halogen, $C_1\text{-}C_{10}$ alkyl ether, heterocyclyl, carbonyl, oxime, $-N(R^1)$ (SO₂R), -C(NNR²R⁴)R¹, $-COOR^1$, $-CONR^2R^2$, -OC(O)R¹, -OC(O)OR¹, -OC(O)NR¹R², $-NR^3C$ (O)R³, $-NR^3C$ (O)OR³, and $-NR^3C$ (O)NR¹R², wherein

R is selected from C_1-C_6 alkyl, trifluoromethyl, phenyl, and substituted phenyl;

20 R^1 and R^2 are independently selected from hydrogen, C_1 - C_{10} alkyl, aryl, heterocyclyl, and alkylaryl, or R^1 and R^2 may be taken together to form a 5- to 10-member ring; and

 R^3 and R^4 are independently selected from hydrogen, C_1 - C_{10} alkyl, aryl, heterocyclyl, alkylaryl, -C(O) R^1 , or -C(O) R^2R^2 ;

 Z^1 is selected from hydrogen, C_1 - C_6 alkyl, aryl, heterocyclyl, $COOR^1$, $CONR^1R^2$, OH, C_1 - C_6 alkyl ether, - $OC(O)R^1$, - $OC(O)OR^1$, - $OC(O)NR^1R^2$, - OR^1R^2 , - $OR^3C(O)R^1$, -

ORT-1527

 $NR^3C(0)OR^1$, $-NR^3C(0)NR^1R^2$, halogen, $-C(0)R^1$, $-C(NR^3)R^1$, $-C(NOR^3)R^2$, and $-C(NNR^3R^4)R^2$;

 $\rm Z^2$ is selected from hydrogen, halogen, $\rm C_1\text{-}C_6$ alkyl;

 \boldsymbol{Z}^{1} and \boldsymbol{Z}^{2} may together form a fused aromatic ring;

n is an integer from 0 to 3;

10 G is selected from $-COOR^1$, $-C(O)COOR^1$, $-CONR^1R^2$, $-CF_3$, $-P(O)(OR^1)(OR^2)$, $-S-R^8$, $-O-R^8$,

-}-COOR²

15

R⁵ and R⁶ are independently hydrogen or C₁-C₆ alkyl;

$$\overset{R^6}{\overset{}{\bigvee}}, \overset{R^7}{\overset{}{\overset{}{\bigvee}}}, \text{ and } \overset{R^7}{\overset{}{\overset{}{\bigvee}}} \text{ wherein }$$

R7 is hydrogen, C1-C6 alkyl, or -C(O)R5;

 R^8 is selected from the group consisting of hydrogen, $C_1 - C_6$ alkyl, and substituted $C_1 - C_6$ alkyl; and

B is oxygen or -NR5;

E is selected from hydrogen, $\text{C}_1\text{--}\text{C}_6$ alkyl and a moiety of the formula

5 X is hydrogen or oxygen, with the proviso that

when E is hydrogen and G is -COOH, -COOCH $_{\!\scriptscriptstyle 3}$, or a moiety of the formula of

A is selected from the group consisting of aryl, heterocyclyl, substituted $C_1\text{-}C_6$ alkyl and $C_7\text{-}C_{10}$ alkyl, provided that when X is hydrogen, n is 1 and G is a moiety of the formula of

A is selected from the group consisting of heterocyclyl, and C₇-C₁₀ alkyl.

2. A compound of Claim 1 wherein

- 20 A is selected from aryl, heterocyclyl, and C₁-C₁₀ alkyl, said aryl, heterocyclyl, and C₁-C₁₀ alkyl being optionally substituted with one or more members selected from the group consisting of halogen, OH, aryl, C₃-C₈ cycloalkyl, C₁-C₁₀ alkyl substituted with a halogen, C₁-C₁₀ alkyl ether,
- 25 heterocyclyl, carbonyl, oxime, -C(NNR³R⁴)R¹, -COOR¹, -CONR¹R², -OC(O)R¹, -OC(O)OR¹, -OC(O)NR¹R², -NR³R², -NR³C(O)R¹, -NR³C(O)OR¹, and -NR³C(O)NR¹R², wherein

 R^1 and R^2 are independently selected from hydrogen, $C_1\text{-}C_{10}$ alkyl, aryl, heterocyclyl, and alkylaryl, or R^1 and R^2 may be taken together to form a 5- to 10-member ring; and

 R^3 and R^4 are independently selected from hydrogen, $C_1\text{-}C_{10}$ alkyl, aryl, heterocyclyl, alkylaryl, -C(O) R^3 , or -C(O) NR^3R^2 ;

10 and

5

G is selected from -COOR¹, -C(O)COOR¹, -CONR²R², -CF₃, -P(O)(OR¹)(OR²), --S-R³,

 R^{5} and R^{6} are independently hydrogen or C_{1} - C_{6} alkyl;

$$\begin{array}{c} R^{g} \\ O \\ N \\ O \end{array}, \quad \begin{array}{c} R^{7} \\ N \\ \end{array}, \quad \text{and} \quad \begin{array}{c} R^{7} \\ N \\ N \\ \end{array}$$
 wherein

 R^7 is hydrogen, C_1 - C_6 alkyl, or -C(0) R^5 ; R^8 is selected from the group consisting of hydrogen, C_1 - C_6 alkyl, and substituted C_1 - C_6 alkyl; and

20

25

B is oxygen or -NR5.

- 3. A compound of Claim 1 wherein X is oxygen.
- 5 4. A compound of Claim 1 wherein E is $C_1\text{-}C_6$ alkyl or a moiety of the formula

$$(\operatorname{CH}_2)_n$$

wherein G and n are as claimed in Claim 1.

- 10 5. A compound of Claim 1 wherein A is optionally substituted C_1 - C_6 alkyl or optionally substituted aryl.
 - 6. A compound of Claim 5 wherein A is substituted $C_1\text{-}C_6$ alkyl and G is -COOH or -COOCH $_1.$
 - 7. A compound of Claim 1 wherein
 - $\mathbb A$ is optionally substituted $C_1\text{-}C_6$ alkyl or optionally substituted aryl;
 - X is oxygen; and

G is selected from $-COOR^1$, $-CONR^1R^2$, $-CF_3$,

$$P\left(O\right)\left(OR^{1}\right)\left(OR^{2}\right),\ \ -S-R^{8},\ \ -O-R^{8},\ \ and$$

8. A compound of Claim 7 wherein

A is $C_1\text{--}C_6$ alkyl or aryl, said $C_1\text{--}C_6$ alkyl or aryl being optionally substituted with one or more

10

members selected from the group consisting of halogen, OH, aryl, C_3 - C_8 cycloalkyl, C_1 - C_{10} alkyl substituted with a halogen, C_1 - C_{10} alkyl ether, heterocyclyl, carbonyl, oxime, -C(NNR 3 R 4)R 1 , -COOR 1 , -CONR 3 R 2 , -OC(O)R 1 , -OC(O)OR 1 , -OC(O)NR 3 R 2 , -NR 3 R 2 , -NR 3 C(O)R 1 , -NR 3 C(O)OR 1 , and -NR 3 C(O)NR 3 R 2 ; and

9. A compound of Claim 1 which is selected from

- 15 10. A pharmaceutical composition comprising a compound of Claim 1 and a pharmaceutically acceptable carrier.
 - 11. A method of treating a subject suffering from a disorder in glucose and lipid metabolism, which comprises

ORT-1527

administering to the subject a therapeutically effective amount of a compound of Claim 1.

- 12. A method of inhibiting in a subject the onset of a 5 disorder in glucose and lipid metabolism, which comprises administering to the subject a prophylactically effective dose of a compound according to Claim 1.
- 13.A method of Claim 11 or 12 wherein said disorder is a 10 condition of reduced insulin sensitivity.
 - 14.A method of Claim 13 wherein said condition of reduced insulin sensitivity is Non-Insulin Dependant Diabetes Mellitus.

15

20

- 15.A method of Claim 11 or 12 wherein said disorder is selected from Non-Insulin Dependant Diabetes Mellitus, obesity, nephropathy, neuropathy, retinopathy, atherosclerosis polycystic ovary syndrome, ischemia, hypertension, stroke, and heart disease.
- 16.A method of Claim 15 wherein said condition is Non-Insulin Dependant Diabetes Mellitus.
- 25 17.A method of Claim 15 wherein said condition is obesity.
 - 18.A method of Claim 15 wherein said condition is hypertension.

30

19.A process for making a pharmaceutical composition comprising mixing any of the compounds according to Claim 1 and a pharmaceutically acceptable carrier.